endonuclease sites, Class III I-endonuclease sites, Class IV I-endonuclease sites, and Class V I-endonuclease sites.

70. The method of claim 69, wherein said endonuclease recognition site is a Class I I-endonuclease site.

71. The method of claim 70, wherein said endonuclease recognition site is selected from the group consisting of I-*Sce*I, I-*Sce*IV, I-*Csm*I, and I-*Pan*I sites.

72. The method of claim 71, wherein said endonuclease recognition site is an I-*Sce*I site. --

REMARKS

Reconsideration of this application is respectfully requested. New claims 48-72 are derived from canceled claims 23-47 and are fully supported by the specification. No new matter is added by amendment. Upon amendment, claims 48-72 are pending in this application.

The Office provisionally rejected claims 23, 24, 27, 28, 31, 32, and 39 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 15, 18, 21, and 28 of copending Application No. 08/643,732. Since this is a provisional rejection, applicants respectfully request that the rejection be held in abeyance until allowable subject matter is indicated.

The Office rejected claims 23-47 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter, which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the claimed invention. The

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Office contends that the specification fails to disclose any transgenic animal comprising a nucleotide sequence encoding I-*Sce* I, wherein the I-*Sce* I is introduced by homologous or non-homologous recombination. The Office also contends that applicants fail to point out where the specification teaches the generation of D3 embryonic stem cells encoding I-*Sce* I. The Office maintains that Viville, 1997, teaches that genetic modulation via homologous recombination is a highly unpredictable art, which requires numerous steps. The Office concludes that, considering the unpredictability in the transgenic art, undue experimentation would be required for the skilled artisan to practice applicants' invention.

Applicants traverse the rejection. Applicants are not required to disclose a working example of the claimed invention. *See Gould v. Quigg,* 822 F.2d 1074, 1078, 3 U.S.P.Q.2d 1302, 1304 (Fed. Cir. 1987). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Furthermore, the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *Id.* In addition, the Federal Circuit has found that screening is not to be equated with undue experimentation. *See In re Wands*, 858 F.2d 731, 740, 8 U.S.P.Q. 2d 1400, 1404 (Fed. Cir. 1988).

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Although applicants' methods may require screening to detect transgenic animals, the practice of applicants' invention requires only routine screening, which is not to be equated with undue experimentation. *See In re Wands*, 858 F.2d at 740, 8 U.S.P.Q. 2d at 1404. Furthermore, no undue experimentation is required to produce applicants' claimed invention since applicants provide a reasonable amount of guidance with respect to generating the claimed transgenic animals. For example, applicants specifically make reference to the use of transgenic D3 embryonic stem cells containing an I-*Sce* I site in the genome, which are able to generate transgenic mice:

> **Two transgenic cell lines with the I-Sce I site at undetermined locations in the genome are available: 1009 (pluripotent nerve cells, J.F. Nicolas) and D3 (ES cells able to generate transgenic animals).**

(Specification at 38, line 12-16.)

The Office has put forth no reasons to doubt the truth of applicants' assertions regarding the generation of transgenic animals from the D3 cell line. In fact, Viville, 1997, cited by the Office, indicates that **the D3 line is an "excellent" embryonic stem cell line**. Viville at 308, column 1, second paragraph. The Office has put forth no reasons to believe that generation of a transgenic mouse from D3 embryonic stem cells would require anything more than routine experimentation.

Furthermore, on page 319, column 2, paragraph 2, **Viville states: "I am convinced that it is now possible to realise any imaginable genetic manipulation in the mouse."** Nothing in Viville et al. indicates that the generation of transgenic mice, for example from D3 embryonic stem cells, would be unpredictable. Nothing in Viville

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indicates that the generation of applicants' claimed transgenic mice would require anything more than routine experimentation. Accordingly, applicants submit that claims 48-72 are fully enabled, and respectfully request withdrawal of the rejection.

Applicants submit that this application is now in condition for allowance. If the Examiner should disagree, the Examiner is invited to contact the undersigned to discuss any remaining issues.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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